

The progression of corrected myopia

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Abstract

Purpose This study seeks to demonstrate the existence of a feedback loop controlling myopia by comparing the prediction of a feedback model to the actual progression of corrected myopia. In addition to theoretical results, confirming clinical data are presented.

Methods The refraction of 13 continuously corrected myopic eyes was collected over a period of time ranging from 4 to 9 years from the time of their first correction. Refractive data was collected in an optometry office from myopic young subjects from the general population in Boston. Subjects were myopes, ages 2 to 22 at the time of first correction selected randomly from a larger population. All individuals were fully corrected with lenses; new lenses were prescribed every time that their myopia increased by 0.25 diopters or more. Subjects wore their spectacle lenses during the followed period.

Results Subjects exhibit a linear time course of myopia progression when corrected with lenses. The observed rate of myopia increase is 0.2 to 1.0 diopters/year, with a mean correlation coefficient $r = -0.971$, $p < 0.005$.

Conclusions This report establishes that feedback control theory applies to the clinical phenomenon of progressive myopia. Continuous correction of myopia results in a linear progression that increases myopia. The Laplace transformation of temporal refractive data to the s-domain simplifies the study of myopia and emmetropia. The feedback transfer function predicts that continuous correction of myopia results in a linear progression because continuous correction opens the feedback loop. This prediction is confirmed with all subjects.

Keywords Emmetropia · Emmetropization · Refraction · Laplace transform · Feedback · Myopia

Introduction

Myopia affects about one third of the world population [1]. The intriguing question of the etiology of myopia development has eluded many investigations. Several facts are now established that allows us an understanding of refraction development of the eye as a system.

Emmetropization and refractive development is a feedback process in humans [2, 3, 5]. There is now considerable evidence showing that there is feedback control of emmetropization in humans and animals, and that refractive development can be manipulated experimentally [4].

The temporal development of the refractive error of the eye can serve to infer the transfer function of the mechanism responsible for such a response.

Medina and Fariza observed an exponential development of refractive error. An exponential development is the response of a first-order feedback system, Fig. 1, to a constant-level step input signal [5]. The input signal or stimulus defines the complete system by observation of the response or output. Input and output time functions are translated to the s-domain by Laplace transformation. The system transfer function is the ratio of the output and input in the s-domain. Such a transfer function will quantitatively model not only the mechanism of emmetropization, but also the effect of lenses.

The refraction of the eye is alterable with external stimuli, supporting the existence of an input signal [4, 6–9]. Corrective lenses applied to the eye are step input stimuli to the emmetropization system. Medina and Fariza [5] showed that the response of a first-order feedback system to an input determined by the power of the corrective lenses fits refraction data from ametropic subjects that wore those lenses.

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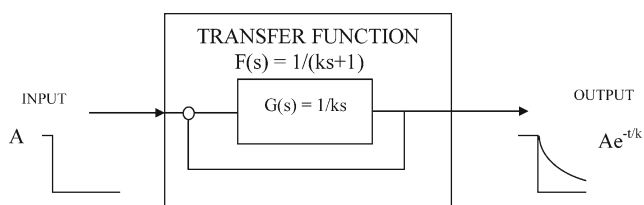


Fig. 1 The transfer function that describes the refractive development of primate eyes is $F(s)=1/(ks+1)$, where k is the time constant of each individual and s is the complex variable. $G(s)=1/ks$ is the forward function of the transfer function. A is the refractive error at birth. The variables are t , time and s , complex variable. The *small circle*, which subtracts output from input, is the error detector

A first order system for emmetropization can be described mathematically with a transfer function $F(s)=1/(ks+1)$, where s is the complex variable and k is the time constant. A system with transfer function $F(s)=1/(ks+1)$ can be represented as a feedback system of unitary feedback and forward or open loop function $G(s)=1/ks$. Fig. 1.

This report shows that Laplace transformation of temporal refractive data to the s -domain is a natural and powerful tool to understand the sophisticated mechanism of emmetropization. The analysis in the Laplace space facilitates the study of the feedback system at work and easily predicts the time course of refractive errors in corrected myopes.

Since the response of a step input is an exponential time course of refractive errors, we can construct the model depicted in Fig. 1. The transfer function of the emmetropization system $F(s)=1/(ks+1)$ produces the observed system output $o(t)=A e^{-t/k}$ if a step input of value A is present; t represents time. The step input A is the initial refractive error or the refractive error at birth. The final level the system seeks is not necessarily zero diopters. That is, emmetropization does not seek perfect emmetropia. It is known that there is a distribution of refractive errors around zero diopters. The distribution is normal at birth and leptokurtic after emmetropization takes place [22]. The uncorrected end refraction is possibly determined genetically. Therefore, emmetropization does not necessarily seek zero diopters as the end point, but some value around it, e.g., -1 diopter for a myope. This is a crucial point to understanding the development of myopia in the first place, and that a low myope will linearly increase his myopia faster once corrected. The system in Fig. 1 does not contain the offset from zero diopters for simplicity. The offset can be achieved with an adder at the output.

Materials and methods

This study involved the retrospective analysis of existing patient records; all identifiers were removed, therefore informed patient consent or IRB approval was not required.

The charts of 185 myopic patients from an optometry clinic in Boston serving the general population were reviewed. Only those (41) who had their first and subsequent full corrections prescribed in the clinic were selected for this study. Further selection criteria were the availability of retinoscopic refractions that were confirmed to agree to ± 0.25 diopters with subjective or automated refraction. All refractions were performed under cycloplegia. No other ocular or systemic comorbidities were present. Twenty-nine patients met these criteria. Two myopes with first refraction greater than 4 diopters at age 7 or younger were excluded. Subjects wore their spectacle lenses during the followed period; compliance was determined by questioning the patients and their parents. Eleven non-compliant patients were excluded. Only subjects with 0.75 or less diopters of astigmatism were included; three subjects exceeding the 0.75 limit were excluded. Subjects were followed from the onset of their myopia or first visit until their last visit; that is, the study includes all the refractions available for the subjects. The time period of data collection was determined to be 2 to 30 years of age, when myopia generally occurs. Lenses were replaced at any visit when the new refraction changed by -0.25 diopters or more. A total of 13 subjects met the above criteria.

Since these subjects wore corrective lenses of the power of their myopic refractive error, a refractive development curve approximated by a single exponential cannot be expected. Instead, a sum of exponentials, determined by the time and extent of each correction, describes their refractive time course, as reported by Medina and Fariza [5].

We can simplify the situation considerably if we assume that corrections were changed continuously. Myopes usually change their corrective lenses when their myopia increases a fraction of a diopter, very frequently during myopia progression, so this assumption is justified. A myope that is fully corrected continuously places the emmetropization feedback system in an open loop condition. Continuous correction alters the feedback loop, effectively rendering it inoperative.

A way to understand that the feedback loop is ineffective is to notice that continuous correction inserts a second, adding feedback loop between output and input. This loop, top in Fig. 2, is necessary because a refractive value at the output

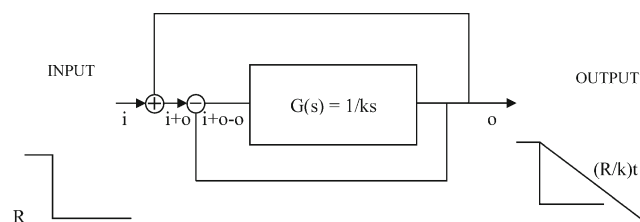


Fig. 2 The transfer function that models continuous correction is $G(s)=1/ks$. The feedback loop in Fig. 1 (*lower loop*) and the loop created by continuous correction (*upper loop*) cancel each other because $i+o-o=i$. The system outputs a *straight line* $(R/k)t$ for a step input of amplitude R . R/k is the slope or rate of myopia progression

results in an immediate correction with the same lens power at the input. The result is zero effect of the two loops because the input is simultaneously added to (continuous correction loop) and subtracted from (original loop) the output.

It can be shown that the open loop transfer function is $G(s)=1/ks$, and the response of the open loop system to a myopic step input is a ramp whose slope is R divided by the time constant k . The former is derived by solving the algebraic equation $F(s)=G(s)/(1+G(s))$, while the latter is derived with the help of the Laplace transform in the following way. The Laplace transform of the step input $i(t)=R$ is $I(s)=R/s$. The output of the system in the Laplace domain is the input times the transfer function or $O(s)=I(s)G(s)=(R/s)(1/ks)=R/ks^2$. The system output in the time domain is the inverse Laplace transform of the output in the s -domain, $o(t)=L^{-1}\{R/ks^2\}=(R/k)t$.

To test the feedback system prediction of a linear response for continuously corrected myopes, we fitted data from the right eyes of the 13 subjects and evaluated the goodness of fit. Choosing only the right eyes is justified because right and left eye refractive errors are highly correlated [10].

Results

Spherical equivalent refractions of the right eyes of the 13 subjects are illustrated in Fig. 3 along with linear regressions. Subjects exhibit a linear time course of myopia progression when corrected with lenses. The least squares straight line regression is a good fit to the data, with slopes

varying from -0.2 to -1.0 diopters/year. The Pearson correlation coefficient r , between the refractive data and age ranges from -0.907 to -0.998 , with a mean $r=-0.971$, $p < 0.005$ for all regressions.

Discussion

The observed results, shown in Fig. 3, agree with the predictions of the first-order feedback system.

Goss [11] also reports that myopia progression follows a straight line between 6 and 15 years of age. He also found, as our model predicts, that refractive changes are greater when a patient is myopic rather than hyperopic or emmetropic. Oakley and Young [12] report, similar to our results, a myopia progression rate of 0.3 to 0.7 diopters/year for fully corrected myopes ages 6 to 17.

According to our model, under-correction of myopia should reduce the progression of myopia only slightly, since the eye is still substantially corrected. Reports of the effect of under-correction, for distance and near, are varied as the following reports exemplify [12–19]. The conflicting results may be due to the small effect of under-correction and the difficulty of the experiment. A problem of these studies where myopes are assigned to groups of fully corrected or under-corrected is that there is a large intersubject variation of the rate of progression of myopia (-0.2 to -1.0 diopters/year in this report).

The feedback model explains adult-onset myopia. There are two subjects with myopia onset at ages 20 and 22, Fig. 3. The linear regressions for these two subjects are excellent ($r=-0.986$, $r=-0.908$). We notice that the

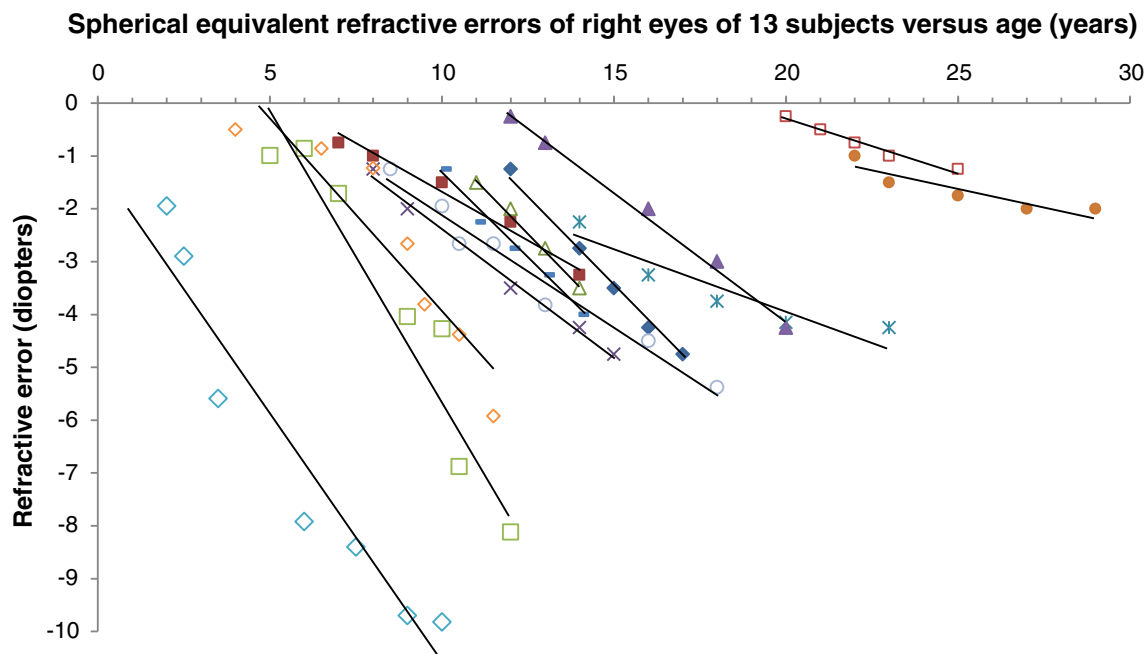


Fig. 3 Refractive errors of right eyes of 13 subjects versus age in years (symbols) and linear regression (solid lines)

difference from the other cases of juvenile myopia is the small slope of the linear regression, indicating a very low rate of progression. Late-onset myopic subjects must have a large emmetropization time constant k because their refraction does not become myopic until their twenties. The model predicts that these subjects will have a small myopic slope R/k as evidenced by our subjects, and as many practitioners have observed. Our two older subjects' last refractions also seem to indicate that stabilization is reached when myopia is still low.

The feedback model is simplified because it does not account for myopia stabilization. Linear progression of myopia cannot continue forever. The feedback model predicts a linear progression of myopia, but it cannot predict when stabilization will occur. There must be a limit, or "saturation" in engineering terms, of the physiological mechanism. This eventual stabilization is observed in progressive myopes [20]. Sometimes stabilization does not occur until adulthood [21]. Some of the subjects in this study also show the beginning of stabilization at their last refraction. The stabilization of myopia can cause some confusion as to the proper fit for specific myopia progressions. An exponential or a double exponent Gompertz curve may fit myopia progression when stabilization is included [20]. While exponential functions may fit refractive development, our results indicate not only that a linear progression is the correct and simplest description for the progression of corrected myopia prior to saturation, but it is supported by a feedback process. The feedback model describes an important phase of myopia, when it is progressing.

This study has several limitations. Although the feedback model accurately describes the progression of myopia in continuously corrected myopes, the model has no predictive power after myopia starts to stabilize. The assumption that myopes are continuously corrected is not valid during stabilization. Our suggestion that younger myopes have a steeper rate of myopia progression is apparent from Fig. 3, but with only 13 subjects we cannot conclude that this is so with confidence. Ong et al. [19] made the same suggestion based on the 3-year myopia progression of 43 partially corrected myopes. The myopia of younger and older subjects could have a different mechanism. Our younger subjects have a slightly lower correlation coefficient, as evidenced by the curvilinear appearance of their data in Fig. 3.

Conclusions

The decaying exponential time course of uncorrected refractive error (emmetropization) becomes a faster linear time course when subjects are corrected. We can conclude that: (1) the course of emmetropization can be altered, (2) the effect of external manipulation on emmetropization, e.g., continuous correction with lenses, can be predicted from the feedback

transfer function, and (3) continuous correction of myopia results in a linear progression that would exacerbate an uncorrected myopia.

Myopia can be modeled as the response of the emmetropization system to a continually changing input. The functional equivalent is the opening of the emmetropization feedback loop. Myopia progression is predicted by our model, and results from such conditions. The meaning of open loop in the temporal domain is that continuous correction of myopia maintains a steady stimulus that emmetropization will try to alter without success. Emmetropization efforts result in myopization, with the only arrest provided by saturation of the physiological mechanism.

The model predicts, and our subjects confirm, that myopes once corrected will fall in a myopia depression of no return, the bottom of the depression being the stabilization floor. This fall from emmetropia to a stabilization floor has been observed in a group of 469 corrected myopic children [20]. The model also explains the skewness towards myopia of the distribution of refractive errors [22]. Of course, leaving a myope uncorrected is not adequate for many people. Delaying the correction of myopia until visual acuity is substantially impaired is however indicated. Such delay will delay the myopia linear decline. Stabilization will then probably occur at the same age as when immediately corrected, resulting in less final myopia.

Myopia is a sophisticated process. Its understanding at a system level, based on its input–output characteristics, may be beneficial and a precursor to detailed knowledge of the physiological mechanism.

Conflict of interest statement The author certifies that he has NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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